REMARKS

With the entry of the present Amendment, claims 1, 5-11, 13-15 and 46 are in this application. Claims 2-4, 12 and 16-45 have been canceled without prejudice, claims 1, 5-10 and 13-14 have been amended for improved clarity, and entry of new claim 46 has been requested None of the amendments made herein constitutes the addition of new matter.

The Drawings

Applicants agree to provide Formal Drawings when the application is in condition for allowance. The Office Action states that Formal Drawings are not required at this time.

Th Requirement for Restriction

The Patent Office has made the requirement fro restriction under 35 U.S.C. 121 final. In view of the finality of the requirement for restriction, Applicants have canceled without prejudice nonelected claims 12 and 16-45.

The Rejections under 35 U.S.C. 112, first paragraph

Claims 1-3, 5-11 and 13-15 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the Specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, has possession of the claimed invention. Applicants respectfully traverse this rejection.

In the interest of advancing prosecution and without acquiescing to the rejection, Applicants have amended claim 1 to recite the features of claims 4 (where the gene or gene fragment comprises the nucleotide sequence set forth in nucleotides 1147-1740 of SEQ ID NO:1. Claims 2-4 have been canceled without prejudice in view of the amendment of claim 1.

Applicants respectfully submit that the recitation of the particular sequence renders this rejection moot, and the withdrawal of the rejection is respectfully requested.

Applicants respectfully submit that the Detailed Description and the Examples demonstrate to one or ordinary skill in the art that the inventors were in possession of the invention as of the filing date. Specifically, Example 6 shows the reverse transcription-polymerase chain reaction of LSU-rRNA using the primer set of SEQ ID NO:5 and SEQ ID NO:6 to determine that the *P. berghei* extra chromosomal genetic element is transcriptionally active. Example 7 shows the assay of blood samples for the presence of Plasmodium spp. is based on 482 *Plasmodium*-infected blood samples using PCR and the primer set of SEQ ID NO:5 and SEQ ID NO:6. In addition, the PCR conditions are presented clearly in Example 7. Importantly, the results in Tables 3-4 show that primer sets (using SEQ ID NO:5 and SEQ ID NO:6) were capable of detecting *P. falciparum*, *P. vivax*, *P. ovale* and *Pl malariae* in 100% of the cases, indicating that this primer is useful in the genus-specific diagnosis of *Plasmodium* infection. Example 9 shows the sequence alignment of rRNA extra chromosomal DNA from various *Plasmodium* species, by using LSU-rRNA fragments cloned in the pGEM-T vector and sequenced. In particular, the comparison of the *Plasmodium* species used in this study showed that this region of the LSU-rRNA gene is highly conserved and that the similarity between *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae* is greater than 91% (see Table 5). It would be readily understood by the skilled artisan that any smaller sequences from within the recited sequence would be effective in the same manner as the 1147 -1740 nucleic acid sequence.

Claims 1-2 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter not described in the Specification in such a way as to enable one skilled in the art to make and/or use the invention. Applicants respectfully traverse this rejection.

In the interest of advancing prosecution and without acquiescing to the rejection, Applicants have amended claim 1 to recite the particular sequence embodied in nucleotides 1147-1740 of SEQ ID NO:1.

In view of the arguments and evidence presented herein and the amendment of claim 1, Applicants respectfully request withdrawal of the rejection.

The Rejections under 35 U.S.C. 112,second paragraph

Claims 1-11 and 13-15 have been rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter Applicants regard as the invention. Applicants respectfully traverse this invention.

Claim 1 recites contacting a biological sample with a probe or primer. The nature of the sample is not defined as a human sample or a blood sample, but as a biological sample. If the biological sample does not contain a human malarial agent, the human malarial agent would not be detected.

In the interest of advancing prosecution and without acquiescing to the rejection, claim 1 has been amended to recite a particular nucleotide sequence which is highly conserved among the human malarial pathogens.

The Patent Office has rightly noted that if the sample does not contain a human malarial agent, the agent would not be detected. This is the point of the claimed method – when the agent is present, it is detected, and where it is absent, it is not. Thus, Applicants respectfully submit that the claim, as currently amended, is abundantly clear to one of skill in the art. If there is a

particular amendment that would make this claim acceptable to the Examiner, Applicants would welcome suggested language.

Claims 2-11 and 13-15 depend from claim 1. The claims before the amendments provided herein recited "or nucleic acid derived therefrom", allegedly referring to the sample, *P. berghei* probe or primer extra chromosomal element and *P. berghei*. The phrase does not clearly define what the derived nucleic acid is as the source of the sample is not defined, etc. Claims 2-11 and 13-14 are allegedly unclear based upon dependence on claim 1.

Claim 2 defines the extra chromosomal genetic element to be a plastid or plastid-like molecule. Clarification has been requested.

In view of the amendment of claim 1 to recite a particular sequence embodied in the probe or primer, claim 2 has been canceled as redundant.

Claim 3 recited "LSU". The full recitation is required.

In view of the amendment of claim 1 to recite a particular sequence embodied in the probe or primer, claim 3 has been canceled as redundant.

Claim 4 recites "wherein the probe or primer comprises an LSU rRNA gene or gene fragment ....", and further clarification has been requested. Claim 4 recites "an LSU-rRNA gene, which allegedly does not further limit claim 3, from which it depends. Claim 4 is further allegedly drawn to a non-elected invention and the elected invention is said to be not distinctly claimed.

In view of the amendment of claim 1 to recite a particular sequence embodied in the probe or primer, claim 4 has been canceled without prejudice, rendering these aspects of the rejections under 35 U.S.C. 112, second paragraph, moot.

Claim 8 allegedly seeks to limit claim 1 by defining the detection means, reciting a methods step, a combination of structural components with specific relationships and a reporter molecule. The methods steps recite identifying a signal produced, but the reporter molecule is said to be capable of producing a signal. Clarification is requested.

In the interest of advancing prosecution and without acquiescing to the rejection, claim 8 has been amended to recite that the reporter molecule produces a signal. Applicants respectfully submit that this amendment renders the claim abundantly clear to the skilled reader. In addition, the exemplary reference to biotin has been deleted. New claim 46 recites the use of biotin as reporter.

Claim 10 allegedly broadens the scope of claim 1 by defining primers or primer pairs to be Plasmodium genus specific and are not limited to the conserved sequences of the probe or primer recited in claim 1. Claim 10 sets forth a combination of probes or primers which is not the single probe or primer of claim 1.

In the interest of advancing prosecution and without acquiescing to the rejection, claim 1 has been amended to recite particular sequence, and claim 10, in the interest of advancing prosecution and without acquiescing to the rejection, has been amended to delete the recitation related to primers.

Claim 11 recites "wherein the PCR format comprises RT-PCR". The Patent has questioned what is amplified when the claimed format does not set forth an RNA reagent.

In the interest of advancing prosecution and without acquiescing to the rejection, claim 11 has been amended to recite that the PCR format is RT-PCR. Applicants respectfully submit that this clarifies the claim. One of skill in the art understands that a positive result with RT-PCR is dependent on the present of RNA in the sample being tested using the RT-PCR method, and it is urged that the claim is definite.

Claim 13 has been objected to for improper Markush recitation.

In the interest of advancing prosecution and without acquiescing to the rejection, claim 13 has been amended to recite selected from the group consisting of", in accordance with accepted practice.

In view of the amendments to the claims and the clarifications provided above, Applicants respectfully urge that the claims be found in compliance with 35 U.S.C. 112, second paragraph, and the rejections be withdrawn.

The Rejections under 35 U.S.C. 102

Claims 1-2, 5-7, 8-10 and 13-14 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by Ayyanathan et al. (1996). Applicants respectfully traverse this rejection.

In the interest of advancing prosecution and without acquiescing to this rejection, claim 1 has been amended to specify the particular sequence of the probe or primer used in the detection methods, namely, nucleotides 1147-1740 of SEQ ID NO:1.

Applicants respectfully submit that the cited Ayyanathan reference described the identification and characterization of a generic DNA probe capable of detecting plasmodial

infections in blood. However, this reference neither reaches nor suggests the use of plastid extra chromosomal DNA sequences in detection methods nor does it teach or suggest the sequence of the probe or primer as set forth within claim 1, as amended, for use in diagnostic methods.

In view of the foregoing discussion and the amendment to the claims, Applicants respectfully maintain that the invention as now claimed is not anticipated by the cited Ayyanathan reference, and withdrawal of the rejection is requested.

Claims 1, 5-8 and 13-14 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by McCutchan et al. (U.S. Patent No. 4,707,445). Applicants respectfully traverse this rejection.

In the interest of advancing prosecution and without acquiescing to this rejection, claim 1 has been amended to specify the particular sequence of the probe or primer used in the detection methods, namely, nucleotides 1147-1740 of SEQ ID NO:1.

The '445 patent describes the isolation of functionally intact whole genes to derive mRNA, sRNA, tRNA, polypeptides and the like. This patent neither teaches nor suggests the method of detecting Plasmodium malarial agents using conserved regions in Plasmodium species nor does it teach or suggest the specifically recited sequences of the probe or primer as set forth in amended claim 1.

In view of the foregoing discussion and the amendment to the claims, Applicants respectfully maintain that the invention as now claimed is not anticipated by the cited McCutchan reference, and withdrawal of the rejection is requested.

Claims (generic) 1, 5-9 and 13-14 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by McCutchan et al. (Science, 1984). Applicants respectfully traverse this rejection.

In the interest of advancing prosecution and without acquiescing to this rejection, claim 1 has been amended to specify the particular sequence of the probe or primer used in the detection methods, namely, nucleotides 1147-1740 of SEQ ID NO:1.

The cited McCutchan paper describes the evolutionary relatedness of Plasmodium species, as determined by DNA structure. This document neither teaches nor suggests the use of plastid extra chromosomal DNA or the sequence of the probe or primer as recited in amended claim1.

In view of the foregoing discussion and the amendment to the claims, Applicants respectfully maintain that the invention as now claimed is not anticipated by the cited McCutchan reference, and withdrawal of the rejection is requested.

Claims (generic) 1, 5-6 and 13-14 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by McCutchan et al. (1988). Applicants respectfully traverse this rejection.

In the interest of advancing prosecution and without acquiescing to this rejection, claim 1 has been amended to specify the particular sequence of the probe or primer used in the detection methods, namely, nucleotides 1147-1740 of SEQ ID NO:1.

This cited McCutchan reference disclosed the sequencing of two 18C ribosomal RNA genes from *Plasmodium falciparum* and comparison to *Plasmodium berghei*. This reference discloses the sue of genomic DNA, not extra chromosomal DNA and the intention set forth was to develop probes which are developmental stage specific and not necessarily ubiquitous to all malarial agents.

This document neither teaches nor suggests the sequence specifically set forth in the amended claims.

In view of the foregoing discussion and the amendment to the claims, Applicants respectfully maintain that the invention as now claimed is not anticipated by the cited McCutchan reference, and withdrawal of the rejection is requested.

Claims (generic) 1, 5-9 and 13-14 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by Das et al. (1996). Applicants respectfully traverse this rejection.

In the interest of advancing prosecution and without acquiescing to this rejection, claim 1 has been amended to specify the particular sequence of the probe or primer used in the detection methods, namely, nucleotides 1147-1740 of SEQ ID NO:1.

The cited Das references discloses a one-step lysis procedure for 18C rRNA-based diagnosis of plasmodial infection. This document does not teach or suggest the sequence of the probe or primer recited within amended claim 1.

In view of the foregoing discussion and the amendment to the claims, Applicants respectfully maintain that the invention as now claimed is not anticipated by the cited Das reference, and withdrawal of the rejection is requested.

Claims (generic) 1 and 13 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by Gardner et al. (1994). Applicants respectfully traverse this rejection.

In the interest of advancing prosecution and without acquiescing to this rejection, claim 1 has been amended to specify the particular sequence of the probe or primer used in the detection methods, namely, nucleotides 1147-1740 of SEQ ID NO:1.

This cited Gardner reference describes the identification of nine putative trn genes in the plastid-like circular DNA of *Plasmodium falciparum* using a DAN probe made by PCR across the cluster of trn genes and specific for the circular DNA in Southern blots of total parasite DNA. This reference does not teach or suggest the sequence of the probe or primer as recited in amended claim 1.

In view of the foregoing discussion and the amendment to the claims, Applicants respectfully maintain that the invention as now claimed is not anticipated by the cited Gardner reference, and withdrawal of the rejection is requested.

Claims (generic) 1-3, 5-10 and 14-15 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by Obst et al. (1990). Applicants respectfully traverse this rejection.

In the interest of advancing prosecution and without acquiescing to this rejection, claim 1 has been amended to specify the particular sequence of the probe or primer used in the detection methods, namely, nucleotides 1147-1740 of SEQ ID NO:1.

The cited Obst reference describes the detection of EDNA sequences in *P. berghei* using a non-radioactive in situ hybridization technique. This document does not teach or suggest the detection of malarial agents using a probe or primer as defined in amended claim 1.

In view of the foregoing discussion and the amendment to the claims, Applicants respectfully maintain that the invention as now claimed is not anticipated by the cited Obst reference, and withdrawal of the rejection is requested.

Claims (elected species) 1, 3-4, 8-10 and 13 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by Gardner et al. (1993). Applicants respectfully traverse this rejection.

In the interest of advancing prosecution and without acquiescing to this rejection, claim 1 has been amended to specify the particular sequence of the probe or primer used in the detection methods, namely, nucleotides 1147-1740 of SEQ ID NO:1.

The cited 1993 Gardner reference discloses a sequence of LSU-rRNA from the 35 kb circular extra chromosomal DNA of *P. falciparum.* The sequence analysis attached to the front of the paper shows the sequence (Accession No. X61660) to be highly conserved wit5h SEQ ID NO:1 within the present application. This reference states that the intention of the research reported therein was to determine the provenance of the circular DNA derived from *P. falciparum.* There is not disclosure of a method for detecting human malarial agents within biological material, and furthermore, this reference does not teach or suggest that the deposited sequence is conserved across the genus of malarial agents, nor is there any disclosure of detection of other human malarial agents, namely *P. vivax*, *P. ovale*, *P. malariae* or *P. falciparum.* Therefore, this reference could not have anticipated that the present methods of detection as claimed.

In view of the foregoing discussion and the amendment to the claims, Applicants respectfully maintain that the invention as now claimed is not anticipated by the cited Gardner reference, and withdrawal of the rejection is requested.

Conclusion

This Amendment is accompanied by a Petition for Extension of Time (two months) and a check in the amount of $205.00 as required by 37 C.F.R. 1.16. It is believed that the present submission does not require the payment of any additional fees under 37 C.F.R. 1.16-1.17. If this is incorrect, please charge any deficiency or credit any overpayment due under the foregoing Rules to Deposit Account No. 07-1969.

Respectfully submitted

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